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|------|-------|------|-------|------|---|
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| NE | WS | 3 | MAR | 31 | CAS REGISTRY enhanced with additional experimental spectra |
| NE | WS | 4 | MAR | 31 | CA/CAplus and CASREACT patent number format for U.S. |
| | | - | | - | applications updated |
| NE | WS | 5 | MAR | 31 | LPCI now available as a replacement to LDPCI |
| NE | WS | 6 | MAR | 31 | EMBASE, EMBAL, and LEMBASE reloaded with enhancements |
| NE | WS | 7 | APR | 04 | STN AnaVist, Version 1, to be discontinued |
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| | | | APR | | IMSRESEARCH reloaded with enhancements |
| NE | WS | 11 | MAY | 30 | INPAFAMDB now available on STN for patent family searching |
| NE | WS | 12 | MAY | 30 | DGENE, PCTGEN, and USGENE enhanced with new homology sequence search option |
| NE | ws | 13 | JUN | 06 | EPFULL enhanced with 260,000 English abstracts |
| | | | JUN | | KOREAPAT updated with 41,000 documents |
| NE | WS | 15 | JUN | 13 | USPATFULL and USPAT2 updated with 11-character |
| | | | | | patent numbers for U.S. applications |
| NE | WS | 16 | JUN | 19 | CAS REGISTRY includes selected substances from |
| 3.15 | WS | 17 | JUN | 2.5 | web-based collections CA/CAplus and USPAT databases updated with IPC |
| NE | IWS | 1/ | JUN | 25 | reclassification data |
| NE | WS | 18 | JUN | 30 | AEROSPACE enhanced with more than 1 million U.S. |
| | | | | | patent records |
| NE | WS | 19 | JUN | 30 | EMBASE, EMBAL, and LEMBASE updated with additional |
| | | | | | options to display authors and affiliated |
| | | | ***** | 2.0 | organizations |
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| 2.17 | WS | 21 | JUN | 20 | Assistant and BLAST plug-in STN AnaVist enhanced with database content from EPFULL |
| | WS | | JUL | | CA/CAplus patent coverage enhanced |
| | | | | | |
| NE | WS | 23 | JUL | 28 | EPFULL enhanced with additional legal status information from the epoline Register |
| MIE | TTC | 24 | JUL | 20 | IFICDB, IFIPAT, and IFIUDB reloaded with enhancements |
| | WS | | JUL | | STN Viewer performance improved |
| | | | | | |
| NE | WS | 26 | AUG | UΙ | INPADOCDB and INPAFAMDB coverage enhanced |
| ME | THIS. | EYPI | PESS | THIN | 27 08 CURRENT WINDOWS VERSION IS V8.3, |
| 145 | 1110 | DACI | ددد | | CURRENT DISCOVER FILE IS DATED 23 JUNE 2008. |
| | | | | THAD | CORREST DISCOVER FIRE TO DATED 23 COME 2000. |

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11
chain nodes :
11 12 14 15 18 19 20 21
ring nodes :
1 2 3 4 5 6 7 8 9 10
chain bonds :
2-18 7-11 11-12 14-15 18-19 19-20 20-21
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-10 7-8 8-9 9-10
exact/norm bonds :
2-18 7-11 11-12 14-15 18-19 20-21
exact bonds :
19-20
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-10 7-8 8-9 9-10
isolated ring systems :
containing 1 :
G1:0,S,N,SO2,[*1]
Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:CLASS 12:Atom 14:CLASS 15:CLASS 18:CLASS 19:CLASS 20:CLASS 21:CLASS
Element Count :
Node 12: Limited
   C,C5
   N.N1
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=> d L1 L1 HAS NO ANSWERS L1 STR

1_S 0

G1 O, S, N, SO2, [@1]

Structure attributes must be viewed using STN Express query preparation.

=> s 11 SAMPLE SEARCH INITIATED 17:17:38 FILE 'REGISTRY' SAMPLE SCREEN SEARCH COMPLETED - 486 TO ITERATE

100.0% PROCESSED 486 ITERATIONS 3 ANSWERS SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
PROJECTED ITERATIONS: 8398 TO 11042
PROJECTED ANSWERS: 3 TO 163

L2 3 SEA SSS SAM L1

=> s l1 full

FULL SEARCH INITIATED 17:17:43 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 9633 TO ITERATE

100.0% PROCESSED 9633 ITERATIONS 56 ANSWERS

SEARCH TIME: 00.00.01

L3 56 SEA SSS FUL L1

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ENTRY SESSION
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=> s 13
L4 3 L3
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=> d 14 1- ibib abs hitstr

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L4 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2008 ACS on STN
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ACCESSION NUMBER: 2007:538808 CAPLUS

DOCUMENT NUMBER: 146:501078

TITLE: Preparation of 6-amino-4-(phenylamino)quinazoline

derivatives as tyrosine kinase inhibitors

INVENTOR(S): Ahn, Young-Gil; Kim, Jong Woo; Bang, Keuk Chan; Park, Bum Woo; Kim, Se Young; Lee, Kyungik; Lee, Kyuhang;

Ko, Myoung-Sil; Kim, Han Kyong; Kim, Young Hoon; Kim, Maeng Sup; Lee, Gwan Sun

PATENT ASSIGNEE(S): Hanmi Pharm. Co., Ltd., S. Korea

SOURCE: PCT Int. Appl., 217pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| | TENT I | | | | KIN | D | DATE | | - 1 | APPL | | ION I | DATE | | | | |
|---------------|--------|-----|-----|-----|-----|-----|------|-----|------|------|----------|-------|------|-----|-----|-----|-----|
| WO 2007055514 | | | | | A1 | - | 2007 | 1 | WO 2 | 006- | 20061108 | | | | | | |
| | W: | ΑE, | AG, | AL, | AM, | AT, | AU, | AZ, | BA, | BB, | BG, | BR, | BW, | BY, | BZ, | CA, | CH, |
| | | CN, | CO, | CR, | CU, | CZ, | DE, | DK, | DM, | DZ, | EC, | EE, | EG, | ES, | FI, | GB, | GD, |
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| | | KP, | KZ, | LA, | LC, | LK, | LR, | LS, | LT, | LU, | LV, | LY, | MA, | MD, | MG, | MK, | MN, |
| | | MW, | MX, | MY, | MZ, | NA, | NG, | NI, | NO, | NZ, | OM, | PG, | PH, | PL, | PT, | RO, | RS, |
| | | RU, | SC, | SD, | SE, | SG, | SK, | SL, | SM, | SV, | SY, | ΤJ, | TM, | TN, | TR, | TT, | TZ, |
| | | UA, | UG, | US, | UZ, | VC, | VN, | ZA, | ZM, | zw | | | | | | | |
| | RW: | ΑT, | BE, | BG, | CH, | CY, | CZ, | DE, | DK, | EE, | ES, | FΙ, | FR, | GB, | GR, | HU, | IE, |
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| | | CF, | CG, | CI, | CM, | GA, | GN, | GQ, | GW, | ML, | MR, | NE, | SN, | TD, | TG, | BW, | GH, |
| | | GM, | KE, | LS, | MW, | MZ, | NA, | SD, | SL, | SZ, | TZ, | UG, | ZM, | ZW, | AM, | ΑZ, | BY, |
| | | KG, | KZ, | MD, | RU, | TJ, | TM | | | | | | | | | | |

| KR 2007049572 KR 832594 | A B1 | 20070511 20080527 | KR | 2006-109137 | | 20061106 |
|----------------------------|---------|----------------------|----|-------------|---|----------|
| PRIORITY APPLN. INFO.: | | | | 2005-106506 | | 20051108 |
| OTHER SOURCE(S): | MARPAT | 146:501078 | KR | 2006-109137 | A | 20061106 |

Ι

The title compds. [I; R1-R5 = independently H, HO, halogen, CF3, C1-6 AB alkyl, C1-6 alkoxy, C3-7 cycloalkyl, hydroxy-C1-5 alkyl, C1-6 alkoxy-C1-6 alkyl, NH2, amino-C1-4 alkyl, C1-6 alkylamino, C1-6 alkoxycarbonyl, C1-6 alkoxyaminocarbonyl, aryl-C1-6 alkoxy, heteroaryl-C1-6 alkoxy, or aryl; R6 = H, C1-6 alkyl or di(C1-6 alkyl)amino-C1-6 alkyl; X = (un)substituted C2-6 alkenylcarbonyl or C2-6 alkynylcarbonyl; Z = (un)substituted C1-6 alkoxy, C1-6 alkenyloxy, aryloxy, heterocyclyloxy, or heterocyclyl-C1-6 alkoxy] or pharmaceutically acceptable salts thereof are prepared These inventive quinazoline derivs. as multiplex inhibitors can selectively and effectively inhibit diseases caused by the overactivity of a tyrosine kinase, in particular a vascular endothelial growth factor receptor (VEGFR) or an epithelial cell growth factor receptor (EGFR). The diseases include cancer, diabetes, psoriasis, rheumatoid arthritis, Kaposi's sarcoma, angioma, acute and chronic nephropathy, arterial restenosis, autoimmune disease, acute infection, and eve disease caused by vein abruption. These compds. effectively inhibited the growth of A431 having overexpressed EGFR1 (HER-1) and SK-Br3 having overexpressed EGFR2 (HER-2) at a low drug concentration, while the compds. did not inhibit the growth of SW-620 not having overexpressed EGFR and EGFR2. They also showed an excellent inhibitory effect on VEGFR-2 (KDR), which is an importance factor for inducing angiogenesis. Thus, amidation of 4-[6-amino-4-(4bromo-2-fluorophenylamino)quinazolin-7-yloxymethyl]piperidine-1-carboxylic acid tert-Bu ester by acryloyl chloride in CH2Cl2 at room temperature for 2 h qave 4-[6-acryloylamino-4-(4-bromo-2-fluorophenylamino)quinazolin-7yloxymethyl]piperidine-1-carboxylic acid tert-Bu ester which was deprotected by treatment with CF3CO2H in CH2Cl2 and acetylated by acetyl chloride in CH2Cl2 at room temperature for 2 h to give N-[7-(1-acetylpiperidin-4-

ylmethoxy)-4-(4-bromo-2-fluorophenylamino)quinazolin-6-yl]acrylamide (II). II showed IC50 of 0.085, 0.048, 0.283, and 3.058 µM against HUVBC, A431, SKBr3, and SW-620 cancer cell lines, resp., and 0.131 and 0.003 µM against VEGFR-2 (KDR) and EGFR-1 (HER-1), resp.

IIT 936558-91-7P, [2-[[4-[(6-Chloropyridin-3-yl)amino]-6nitroquinazolin-7-yl]oxy]ethyl]carbamic acid tert-butyl ester 936558-92-8P, [7-(2-Aminoethoxy)-6-nitroquinazolin-4-yl](6chloropyridin-3-yl)amine 936558-93-9P, N-[2-[[4-[(6Chloropyridin-3-y1)amino]-6-nitroquinazolin-7-y1]oxy]ethy1]acetamide

936558-94-0P, N-[2-[[6-Amino-4-[(6-chloropyridin-3-

yl)amino]quinazolin-7-yl]oxy]ethyl]acetamide

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of 6-amino-4-(phenylamino)quinazoline derivs. as tyrosine kinase inhibitors)

RN 936558-91-7 CAPLUS

CN Carbamic acid, N-[2-[[4-[(6-chloro-3-pyridinyl)amino]-6-nitro-7-quinazolinyl]oxy]ethyl]-, 1,1-dimethylethyl ester (CA INDEX NAME)

RN 936558-92-8 CAPLUS

CN 4-Quinazolinamine, 7-(2-aminoethoxy)-N-(6-chloro-3-pyridinyl)-6-nitro-(CA INDEX NAME)

RN 936558-93-9 CAPLUS

CN Acetamide, N-[2-[[4-[(6-chloro-3-pyridinyl)amino]-6-nitro-7-quinazolinyl]oxy]ethyl]- (CA INDEX NAME)

- RN 936558-94-0 CAPLUS
- CN Acetamide, N-[2-[[6-amino-4-[(6-chloro-3-pyridiny1)amino]-7quinazoliny1]oxy]ethy1]- (CA INDEX NAME)

- II 936558-89-3P, N-[7-(2-Acetylaminoethoxy)-4-[(6-chloropyridin-3yl)amino]quinazolin-6-yl]acrylamide Rl: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 - (preparation of 6-amino-4-(phenylamino)quinazoline derivs. as tyrosine kinase inhibitors)
- RN 936558-89-3 CAPLUS
- CN 2-Propenamide, N-[7-[2-(acetylamino)ethoxy]-4-[(6-chloro-3pyridinyl)amino]-6-quinazolinyl]- (CA INDEX NAME)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:566625 CAPLUS DOCUMENT NUMBER: 141:123758

TITLE: Preparation of phosphonooxy quinazoline derivatives as

therapeutic agents
INVENTOR(S): Mortlock, Andrew Austen

PATENT ASSIGNEE(S): Astrazeneca Ab, Swed.; Astrazeneca Uk Limited

SOURCE: PCT Int. Appl., 97 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| 1 | | ENT | | | | KIN | | | | | | ICAT | | DATE | | | | | |
|-------|----------------------|-------|------|-----|-----|-----------|-----|------|------|----------------|------|------|------|------|------------|----------|------|-----|----|
| 1 | | | | | | A1 200407 | | | | | | | | | | | | | |
| | | | | | | | | | | | | BG, | | | | | | | |
| | | | | | | | | | | | | EC, | | | | | | | |
| | | | | | | | | | | | | JP, | | | | | | | |
| | | | | | | | | | | | | MK, | | | | | | | |
| | | | | | | | | | | | | SD, | | | | | | | |
| | | | | | | | | | | | | | | | | | | 10, | |
| | | | | | | | | | | | | VC, | | | | | | | |
| | | RW: | | | | | | | | | | SZ, | | | | | | | |
| | | | BY, | KG, | ΚZ, | MD, | RU, | ТJ, | TM, | ΑT, | BE, | BG, | CH, | CY, | CZ, | DE, | DK, | EE, | |
| | | | ES, | FI, | FR, | GB, | GR, | HU, | ΙE, | IT, | LU, | MC, | NL, | PT, | RO, | SE, | SI, | SK, | |
| | | | TR, | BF, | ВJ, | CF, | CG, | CI, | CM, | GA, | GN, | GQ, | GW, | ML, | MR, | NE, | SN, | TD, | TG |
| | ΑU | 2003 | 2941 | 42 | | A1 | | 2004 | 0722 | AU 2003-294142 | | | | | | 20031222 | | | |
| 1 | EΡ | 1575 | 966 | | | A1 | | 2005 | 0921 | | EP 2 | 003- | 7895 | | 20031222 | | | | |
| | | R: | AT, | BE, | CH, | DE, | DK, | ES, | FR, | GB, | GR, | IT, | LI, | LU, | NL, | SE, | MC, | PT, | |
| | | | IE. | SI. | LT. | LV. | FI. | RO. | MK. | CY. | AL. | TR, | BG. | CZ. | EE. | HU. | SK | | |
| | JP 2006512387 | | | | | | | | | | | | | | | | | 222 | |
| 1 | US 20060058325 | | | | | | | 2006 | 0316 | | US 2 | 005- | 5394 | 83 | | 2 | 0050 | 617 | |
| PRIOR | IORITY APPLN. INFO.: | | | | | | | | | EP 2 | 002- | 2932 | 40 | | A 20021224 | | | | |
| | | | | | | | | | | | WO 2 | 003- | GB56 | 40 | | W 2 | 0031 | 222 | |
| OTHER | SC | DURCE | (S): | | | MAR | PAT | 141: | 1237 | | | | | | | | | | |

ΙT

RN

CN

Preparation of phosphonooxy quinazoline derivs. I (A = 6-membered heteroary) AR containing nitrogen atom and optionally containing one or two further nitrogen atoms; X = 0, S, S(0), S(0)2, organoamino; m = 0-4; Y = 0, carbonylamido, etc.; Z = organoamino, phosphonooxy, C3-6 (un)substituted phosphonooxy cycloalkyl, etc.; R3 = H, halo, cyano, nitro, C1-6 alkoxy, C1-6 alkyl, carbonylamido, sulfonylamido, organoamino, etc.; R4 = H, C1-4 alkyl, heteroarvl, heteroarvl C1-4 alkvl, arvl, arvl C1-4 alkvl, halo Me Et, cyclopropyl, ethynyl substituted alkyl, etc.), compns. containing them, processes for their preparation and their use in therapy, is described. Thus, reaction of N-{6-[(3-chlorobenzyl)oxy]pyridin-3-yl}-7-(3-chloropropoxy)-6methoxyquinazolin-4-amine (preparation given) with 3-amino-3-methylbutanol in di-Me acetamide in the presence of KI gave 75% 3-[(3-{[4-({6-[(3chlorobenzyl)oxy]pyridin-3-yl}amino)-6-methoxyquinazolin-7yl]oxy}propyl)amino]-3-methylbutan-1-ol which on treatment with di-tert-buty1-N, N-diethylphosphoramidite, oxidation with H2O2, and hydrolysis of the formed phosphate ester gave title compound, 3-[[3-[[4-[[6-[(3-

chlorobenzyl)oxy]pyridin-3-yl]amino]-6-methoxyquinazolin-7-yl]oxy]propyl]amino]-3-methylbutyl dihydrogen phosphate.

722485-20-3p 722485-21-4p 722485-22-5p 722485-26-9p 722485-27-0p 722485-30-5p 722485-32-7p 722485-36-1p 722485-37-2p 722485-34-9p 722485-36-1p 722485-37-2p 722485-39-4p 722485-46-3p 722485-88-5p 722485-97-4p 722485-05-7p 722485-83-8p 722485-97-4p 722486-05-7p 722486-28-4p 722486-37-5p 722486-43-3p 722486-52-4p 722486-59-1p 722486-65-9p 722486-85-3p 722486-33-3p RLi BSU (Biological study, unclassified);

RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (USes)

(preparation of phosphonooxy quinazoline derivs. as the rapeutic agents) $722485 - 20 - 3\,$ CAPLUS

1-Butanol, 3-[[3-[[4-[[6-[(3-chlorophenyl)methoxy]-3-pyridinyl]amino]-6-methoxy-7-quinazolinyl]oxy]propyl]amino]-3-methyl-, dihydrogen phosphate (ester) (9CI) (CA INDEX NAME)

RN 722485-21-4 CAPLUS

CN Benzamide, 3-chloro-N-[5-[[7-[3-[[1,1-dimethyl-3-(phosphonoxy)propyl]amino]propoxy]-6-methoxy-4-quinazolinyl]amino]-2pyridinyl]- (CA INDEX NAME)

RN 722485-22-5 CAPLUS

CN Benzamide, 3-chloro-N-[5-[[7-[3-[ethyl[2-(phosphonooxy)ethyl]amino]propoxy]-6-methoxy-4-quinazolinyl]amino]-2-pyridinyl]- (CA INDEX NAME)

RN 722485-26-9 CAPLUS
CN Benzamide, N-[5-[[7-[3-[ethyl[2-(phosphonooxy)ethyl]amino]propoxy]-6methoxy-4-quinazolinyl]amino]-2-pyridinyl]-3-fluoro (CA INDEX NAME)

RN 722485-27-0 CAPLUS

CN

Benzamide, 3,4-difluoro-N-[5-[[6-methoxy-7-[3-[(1-methylethyl)[2-(phosphonooxy)ethyl]amino]propoxy]-4-quinazolinyl]amino]-2-pyridinyl]-(CA INDEX NAME)

PAGE 2-A

F

RN 722485-30-5 CAPLUS

CN Benzamide, 3-chloro-N-[5-[[6-methoxy-7-[3-[methyl[2-(phosphonooxy)ethyl]amino]propoxy]-4-quinazolinyl]amino]-2-pyridinyl]-(CA INDEX NAME)

RN 722485-32-7 CAPLUS
CN Benzamide, 3-chloro-N-[5-[[7-[[5-[ethyl[2-(phosphonooxy)ethyl]amino]pentyl
]oxy]-6-methoxy-4-quinazolinyl]amino]-2-pyridinyl]- (CA INDEX NAME)

RN 722485-34-9 CAPLUS

CN Benzamide, 3-chloro-N-[5-[[7-[3-[ethyl[4-(phosphonooxy)butyl]amino]propoxy]-6-methoxy-4-quinazolinyl]amino]-2-pyridinyl]- (CA INDEX NAME)

RN 722485-36-1 CAPLUS

CN Benzamide, 3-fluoro-N-[5-[[6-methoxy-7-[3-[methyl[2-[phosphonoxy]ethyl]amino]propoxy]-4-quinazolinyl]amino]-2-pyridinyl]-(CA INDEX NAME)

RN 722485-37-2 CAPLUS

CN Benzamide, 3-chloro-N-[5-[[6-methoxy-7-[3-[(2-methylpropyl)[2-(phosphonooxy)ethyl]amino]propoxy]-4-quinazolinyl]amino]-2-pyridinyl]-(CA INDEX NAME) H2O3PO-CH2-CH2

722485-39-4 CAPLUS

Benzamide, 3-chloro-N-[5-[[7-[3-[cyclopropy1[2-CN (phosphonooxy)ethyl]amino]propoxy]-6-methoxy-4-quinazolinyl]amino]-2pyridinyl]- (CA INDEX NAME)

RN

722485-46-3 CAPLUS Benzamide, 3-chloro-N-[5-[[7-[3-[cyclobuty1[2-CN (phosphonooxy)ethyl]amino]propoxy]-6-methoxy-4-quinazolinyl]amino]-2pyridinyl]- (CA INDEX NAME)

RN 722485-48-5 CAPLUS

CN Benzamide, 3-chloro-N-[5-[[6-methoxy-7-[3-[[2-(phosphonooxy)ethyl]-2propyn-1-ylamino]propoxy]-4-quinazolinyl]amino]-2-pyridinyl]- (CA INDEX NAME)

RN 722485-71-4 CAPLUS

CN 1-Butanol, 3-[[3-[[4-[[6-[(3-chloropheny])methoxy]-3-pyridinyl]amino]-6-methoxy-7-quinazolinyl]oxy]propyl]amino]-3-methyl-, dihydrogen phosphate (ester), dihydrochloride (9C1) (CA INDEX NAME)

$$\begin{array}{c} \text{Me} \\ \text{H}_2\text{O}_3\text{PO}-\text{CH}_2-\text{CH}_2-\text{C}-\text{NH}-\text{(CH}_2)_3-\text{O} \\ \text{Me} \\ \\ \text{Me} \\ \\ \text{N} \\ \\ \text{N} \\ \\ \text{N} \\ \\ \text{N} \\ \\ \text{CH}_2 \\ \\ \\ \text{C1} \\ \\ \end{array}$$

PAGE 2-A

●2 HC1

RN 722485-75-8 CAPLUS

CN Benzamide, 3-chloro-N-[5-[[7-[3-[[1,1-dimethy]-3-(phosphonooxy)propyl]amino]propoxy]-6-methoxy-4-quinazolinyl]amino]-2pyridinyl]-, hydrochloride (1:3) (CA INDEX NAME)

PAGE 2-A

●3 HC1

RN 722485-83-8 CAPLUS

CN Benzamide, 3-chloro-N-[5-[[7-[3-[ethyl[2-(phosphonooxy)ethyl]amino]propoxy]
-6-methoxy-4-quinazolinyl]amino]-2-pyridinyl]-, hydrochloride (1:3) (CA
NDEX NAME)

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●3 HC1

722485-97-4 CAPLUS

RN Benzamide, N=[5-[[7-[3-[ethyl[2-(phosphonooxy)ethyl]amino]propoxy]-6-methoxy-4-quinazolinyl]amino]-2-pyridinyl]-3-fluoro-, hydrochloride (1:3)CN (CA INDEX NAME)

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●3 HC1

RN 722486-05-7 CAPLUS

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●2 HC1

RN 722486-28-4 CAPLUS

CN Benzamide, 3-chloro-N-[5-[[6-methoxy-7-[3-[methyl[2-(phosphonoxy)ethyl]amino]propoxy]-4-quinazolinyl]amino]-2-pyridinyl]-, hydrochloride (1:2) (CA INDEX NAMB)

PAGE 2-A

●2 HC1

RN 722486-37-5 CAPLUS

CN Benzamide, 3-chloro-N-[5-[[7-[[5-[ethyl[2-(phosphonooxy)ethyl]amino]pentyl]oxy]-6-methoxy-4-quinazolinyl]amino]-2-pyridinyl]-, hydrochloride (1:2) (CA INDEX NAME)

PAGE 2-A

●2 HC1

RN 722486-43-3 CAPLUS

CN Benzamide, 3-chloro-N-[5-[[7-[3-[ethyl[4-(phosphonooxy)butyl]amino]propoxy]-6-methoxy-4-quinazolinyl]amino]-2-pyridinyl]-, hydrochloride (1:2) (CA INDEX NAME)

PAGE 2-A

●2 HC1

RN 722486-52-4 CAPLUS

CN Formic acid, compd. with 3-fluoro-N-[5-[6-methoxy-7-[3-[methyl[2-(phosphonooxy)ethyl]amino]propoxy]-4-quinazolinyl]amino]-2-pyridinyl]benzamide (1:1) (CA INDEX NAME)

CM

CRN 722485-36-1

CMF C27 H30 F N6 O7 P

CM

CRN 64-18-6 CMF C H2 O2

О== СН− ОН

RN 722486-59-1 CAPLUS

CN Benzamide, 3-chloro-N-[5-[[6-methoxy-7-[3-[(2-methylpropyl)[2-(phosphonoxy)ethyl]amino]propoxy]-4-quinazolinyl]amino]-2-pyridinyl]-, hydrochloride (1:2) (CA INDEX NAME)

RN 722486-65-9 CAPLUS

CN Benzamide, 3-chloro-N-[5-[[7-[3-[cyclopropyl[2-(phosphonooxy) ethyl]amino[propoxy]-6-methoxy-4-quinazolinyl]amino]-2pyridinyl]-, hydrochloride (1:2) (CA INDEX NAME)

RN 722486-85-3 CAPLUS

CN Benzamide, 3-chloro-N-[5-[[7-[3-[cyclobutyl[2-(phosphonooxy)ethyl]amino]propoxy]-6-methoxy-4-quinazolinyl]amino]-2pyridinyl]-, hydrochloride (1:2) (CA INDEX NAME)

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●2 HC1

722486-93-3 CAPLUS RN CN Benzamide, 3-chloro-N-[5-[[6-methoxy-7-[3-[[2-(phosphonooxy)ethyl]-2propyn-1-ylamino]propoxy]-4-quinazolinyl]amino]-2-pyridinyl]-, hydrochloride (1:2) (CA INDEX NAME)

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722485-73-6P 722485-81-6P 722485-95-2P
722486-03-5P 722486-24-0P 722486-26-2P
722486-35-3P 722486-41-1P 722486-46-6P
722486-49-9P 722486-55-7P 722486-57-9P
722486-61-5P 722486-63-7P 722486-81-9P
722486-83-1P 722486-89-7P 722486-91-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
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(preparation of phosphonooxy quinazoline derivs. as therapeutic agents)

RN 722485-65-6 CAPLUS

CN 1-Butanol, 3-[[3-[[4-[[6-[(3-chlorophenyl)methoxy]-3-pyridinyl]amino]-6methoxy-7-quinazolinyl]oxy]propyl]amino]-3-methyl- (CA INDEX NAME)

- 722485-67-8 CAPLUS RN
- CN Phosphorous acid, 3-[[3-[[4-[[6-[(3-chlorophenyl)methoxy]-3pyridinyl]amino]-6-methoxy-7-quinazolinyl]oxy]propyl]amino]-3-methylbutyl bis(1,1-dimethylethyl) ester (CA INDEX NAME)

RN 722485-69-0 CAPLUS

CN Phosphoric acid, 3-[[3-[[4-[[6-[(3-chloropheny])methoxy]-3-pyridinyl]amino]-6-methoxy-7-quinazolinyl]oxy]propyl]amino]-3-methylbutyl bis(1,1-dimethylethyl) ester (CA INDEX NAME)

RN 722485-73-6 CAPLUS

CN Benzamide, 3-chloro-N=[5-[[7-[3-[(3-hydroxy-1,1dimethylpropyl)amino]propoxy]-6-methoxy-4-quinazolinyl]amino]-2-pyridinyl]-(CA INDEX NAME)

RN 722485-81-6 CAPLUS
CN Benzamide, 3-chloro-N-[5-[[7-(3-[ethyl(2-hydroxyethyl)amino]propoxy]-6methoxy-4-quinazolinyl]amino]-2-pyridinyl] (CA INDEX NAME)

RN 722485-95-2 CAPLUS
CN Benzamide, N-[5-[[7-[3-[ethy1(2-hydroxyethy1)amino]propoxy]-6-methoxy-4quinazolinyl]amino]-2-pyridinyl]-3-fluoro- (CA INDEX NAME)

RN

722486-03-5 CAPLUS
Benzamide, 3,4-diffluoro-N-[5-[[7-[3-[(2-hydroxyethyl)(1-methylethyl)amino]-propoxy]-6-methoxy-4-quinazolinyl]amino]-2-pyridinyl]-CN (CA INDEX NAME)

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RN 722486-24-0 CAPLUS

CN Benzamide, 3-chloro-N-[5-[[7-[3-[(2-hydroxyethyl)methylamino]propoxy]-6-methoxy-4-quinazolinyl]amino]-2-pyridinyl]- (CA INDEX NAME)

RN 722486-26-2 CAPLUS

CN Phosphoric acid, 2-[[3-[[4-[[6-[(3-chlorobenzoy1)amino]-3-pyridiny1]amino]-6-methoxy-7-quinazoliny1)axylpropy1]methylamino]ethyl bis(1,1-dimethylethyl) ester (CA INDEX NAME)

RN 722486-35-3 CAPLUS
CN Benzamide, 3-chloro-N-[5-[[7-[[5-[ethyl(2-hydroxyethyl)amino]pentyl]oxy]-6methoxy-4-quinazolinyl]amino]-2-pyridinyl]- (CA INDEX NAME)

RN 722486-41-1 CAPLUS
CN Benzamide, 3-chloro-N-[5-[[7-[3-[ethyl(4-hydroxybutyl)amino]propoxy]-6methoxy-4-quinazolinyl]amino]-2-pyridinyl]- (CA INDEX NAME)

RN 722486-46-6 CAPLUS
CN Benzamide, 3-chloro-N-[5-[[7-[3-[ethyl[4-(phosphonooxy)butyl]amino]propoxy
]-6-methoxy-4-quinazolinyl]amino]-2-pyridinyl]-, 2,2,2-trifluoroacetate
[1:2] (CA INDEX NAME)

CM 1

CRN 722485-34-9 CMF C30 H36 C1 N6 O7 P

CM 2

CRN 76-05-1 CMF C2 H F3 O2

RN 722486-49-9 CAPLUS

CN Benzamide, 3-fluoro-N-[5-[[7-[3-[(2-hydroxyethyl)methylamino]propoxy]-6-methoxy-4-quinazolinyl]amino]-2-pyridinyl]- (CA INDEX NAME)

Me

RN 722486-55-7 CAPLUS

CN Benzamide, 3-chloro-N-[5-[[7-[3-[(2-hydroxyethyl) (2-methylpropyl) amino]propoxy]-6-methoxy-4-quinazolinyl]amino]-2-pyridinyl]-(CA INDEX NAME)

HO-CH2-CH2

RN 722486-57-9 CAPLUS

CN Phosphoric acid, 2-[[3-[[4-[[6-[(3-chlorobenzoy1)amino]-3-pyridiny1]amino]-6-methoxy-7-quinazoliny1]oxy1propy1)[2-methy1propy1)amino]ethy1 bis(1,1-dimethy1ethy1) ester (CA INDEX NAME)

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RN 722486-61-5 CAPLUS

CN Benzamide, 3-chloro-N-[5-[[7-[3-[cyclopropy1(2-hydroxyethy1)amino]propoxy]-6-methoxy-4-quinazoliny1]amino]-2-pyridiny1]- (CA INDEX NAME)

RN 722486-63-7 CAPLUS

CN Phosphoric acid, 2-[[3-[[4-[[6-[(3-chlorobenzoy1)amino]-3-pyridiny1]amino]-6-methoxy-7-quinazoliny1]oxy1propy1]cyclopropy1amino]ethy1 bis(1,1-dimethylethy1) ester (CA INDEX NAME)

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- RN 722486-81-9 CAPLUS
- CN Benzamide, 3-chloro-N-[5-[[7-[3-[cyclobutyl(2-hydroxyethyl)amino]propoxy]-6-methoxy-4-quinazolinyl]amino]-2-pyridinyl]- (CA INDEX NAME)

RN 722486-83-1 CAPLUS
CN Phosphoric acid, 2-[[3-[[4-[[6-([3-chlorobenzoy1)amino]-3-pyridinyl]amino]-6-methoxy-7-quinazolinyl]oxy]propyl]cyclobutylamino]ethyl
bis(1,1-dimethylethyl) ester (CA INDEX NAME)

RN 722486-89-7 CAPLUS

CN Benzamide, 3-chloro-N-[5-[[7-[3-[(2-hydroxyethyl)-2-propyn-1-ylamino]propoxy]-6-methoxy-4-quinazolinyl]amino]-2-pyridinyl]- (CA INDEX NAME)

RN 722486-91-1 CAPLUS
CN Phosphoric acid, 2-[[3-[[4-[[6-([3-chlorobenzoy1)amino]-3-pyridinyl]amino]-6-methoxy-7-quinazolinyl]oxy]propyl]-2-propyn-1-ylamino]ethyl
bis(1,1-dimethylethyl) ester (CA INDEX NAME)

PAGE 1-A

t-BuO-P-O-CH₂-CH₂
OBu-t
HC== C-CH₂-N-(CH₂)3-O
N
MeO
NH

PAGE 2-A

L4 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2001:228867 CAPLUS

DOCUMENT NUMBER: 134:266318

TITLE: Preparation of quinazolines as aurora 2 kinase

inhibitors

INVENTOR(S): Mortlock, Andrew Austen; Keen, Nicholas John Astrazeneca AB, Swed.; Astrazeneca UK Limited PATENT ASSIGNEE(S):

SOURCE: PCT Int. Appl., 208 pp.

CODEN: PIXXD2 DOCUMENT TYPE: Patent

LANGUAGE: English FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PA' | TENT : | NO. | | KIND DATE | | | | | | API | PLICAT | DATE | | | | | |
|------|---------|---------|------|-----------|--------------------------|------|------|------|-------------|-------|-------------------------|----------|----------|-----|---------|------|-----|
| | | | | | | | | | | 2000- | | | | | | | |
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| | | ΙE, | SI, | LT, | LV, | FI, | RO, | MK, | CY, | ΑI | | | | | | | |
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| ZA | 2002 | 0022 | 32 | | A | | 2003 | 0619 | | ZA | 2002- | 2232 | | | 2 | 0020 | 319 |
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| | 7235 | | | | В1 | | 2007 | 0626 | | US | 2002- | 8885 | 6 | | 2 | 0020 | 321 |
| ORIT | APP | LN. | INFO | .: | | | | | | | 1999- | | | | | | |
| | | | | | | | | | | WO | 2000- | GB35 | 93 | | W 2 | 0000 | 919 |
| ER S | JURCE | (S): | | | MARPAT 134:26631 | | | | | | | | | | | | |

OTHER SOURCE(S): MARPAT 134:266318

GI

- AB Title compds. (I) [wherein X = 0, S, SO, SO2, NH, or NR6; R6 = H or alkyl; R5 = (un)substituted 6-membered aromatic ring containing at least one N; R1-R4
 - independently halo, CN, NO2, alkylsulfanyl, N(OH)R7, or R9X1; R7 = H or alkyl; X1 = a direct bond, O, CH2, OC(O), CO, S, SO, SO2, or (un)substituted NHCO, CONH, SO2NH, NHSO2, or NH; R9 = H or (un)substituted hydrocarbyl, heterocyclyl, or alkoxy; and at least one of R2 or R3 is other than H; or a salt, ester, amide, or prodrug thereof) were prepared as aurora 2 kinase inhibitors for the treatment of proliferative diseases, such as cancer. For example, 2-(N-benzoylamino)-5-aminopyrimidine and 4-chloro-6,7-dimethoxyquinazoline were coupled in i-PrOH to yield II (58%). The latter inhibited the serine/threonine kinase activity of surora 2 kinase by 50% at a concentration of 0.00785 µM. In addition, II gave 50% inhibition of MCF-7 cell proliferation at 1.7 µM and reduced BrdU incorporation into cellular DNA by 50% at 1,92-2,948 µM.
 - IT 331805-82-4P 331805-87-9P 331805-92-6P
- 331806-40-7P RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 - (target compds.; preparation of substituted quinazoline derivs. as inhibitors of aurora 2 kinase for the treatment of breast and colorectal cancers)
- RN 331805-82-4 CAPLUS
- CN 4-Quinazolinamine, N-[6-[(3-chlorophenyl)methoxy]-3-pyridinyl]-6-methoxy-7[3-(4-morpholinyl)propyl]amino[propoxy]- (CA INDEX NAME)

RN 331805-87-9 CAPLUS

CN 1,3-Propanediamine, N3-[3-[[4-[[6-[(3-chlorophenyl)methoxy]-3pyridinyl]amino]-6-methoxy-7-quinazolinyl]oxy]propyl]-N1,N1-dimethyl- (CA INDEX NAME)

RN 331805-92-6 CAPLUS

CN Ethanol, 2-[[3-[[4-[[6-[(3-chloropheny1)methoxy]-3-pyridiny1]amino]-6-methoxy-7-quinazoliny1]oxy]propy1]methylamino]- (CA INDEX NAME)

RN 331806-40-7 CAPLUS
CN 1-Propanol, 2-[[3-[[4-[[6-[(3-chlorophenyl)methoxy]-3-pyridinyl]amino]-6methoxy-7-quinazolinyl]oxy]propyl]amino]-2-methyl- (CA INDEX NAME)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD, ALL CITATIONS AVAILABLE IN THE RE FORMAT

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FILE 'REGISTRY' ENTERED AT 17:17:11 ON 05 AUG 2008

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FILE 'CAPLUS' ENTERED AT 17:17:48 ON 05 AUG 2008 3 S L3 L4

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